UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,704	09/05/2006	Hiromu Habashita	Q90961	4009

65565 7590 12/24/2008

SUGHRUE-265550
2100 PENNSYLVANIA AVE. NW
WASHINGTON, DC 20037-3213

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
12/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,704	HABASHITA ET AL.	
	Examiner	Art Unit	
	NOBLE JARRELL	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,9-15,17 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,9-15,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. The rejections under 35 U.S.C. 112 1st paragraph (written description and scope of enablement) have been overcome by the amendment filed 9/5/2008.

2. The rejections under 35 U.S.C. 102 and 103 have been overcome by the amendment filed 9/5/08.

Claim Objections

3. Claims 1, 3, 9-15, and 17-18 are objected to because of the following informalities: they contain non-elected subject matter. Appropriate correction is required.

Specification

4. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

5. The attempt to incorporate subject matter into this application by reference to a chemokine inhibitor is ineffective because applicants have provided various WIPO documents as references for these agents (see pages 51-52 of the specification). This rejection is maintained because these inhibitors are still considered essential subject matter in these claims.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The issue concerning the meaning of each recited agonist or inhibitor is discussed in the 35 U.S.C. 112, paragraph 2 rejection. Claims 17 and 18 do not contain generic formulae indicating structural makeup for an aldose reductase inhibitor, a cannabinoid-2 receptor agonist, adrenocorticotropic hormone, a metalloproteinase inhibitor, a T-cell inhibitor, a TNF-α inhibitor, an IL-6 inhibitor, an interferon γ agonist, an IL-1 inhibitor, or an NF-κβ inhibitor.

According to the MPEP §2163 I. A. "the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." The MPEP states in §2163 II 3 ii) "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such

identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406."

According to the MPEP §2163.02 Standard for Determining Compliance With the Written Description Requirement, "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter". Ralston Purina Co. v. Far-Mar-Co., Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))."

This case was filed before Applicants had a clear idea of the structures encompassing the scope of claims 17 and 18. The specification provides broad areas of future research and speculation, inviting undue experimentation in learning how to use Applicants' invention.

Applicants are reminded of what the U.S. Court of Appeals Federal Circuit wrote in University of California v. Eli Lilly and Co. 43 USPQ2d 1398, "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic

claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). "It is only a definition of a useful result rather than a definition of what achieves that result." "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")".

8. Claim 15 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vitro* binding of compounds of formula I to CCR1 or CCR5 receptors, does not reasonably provide enablement for treatment of any disease linked to CCR1 or CCR5 binding. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5)

the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to agonism or inhibition of CCR1 or CCR5 receptors with compounds composed of a piperidine ring connected to a phenyl ring, which is further modified with an alkylene-amide-phenyl group. Thus, the claims taken together with the specification imply that these compounds will work *in vivo*.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Pease et al. (*Expert Opinion in Investigational Drugs*, **2005**, *14(7)*, 785-96) teach that CCR1 antagonists do not show efficacy due to bioavailability or the role of CCR1 in pathogenesis. Few compounds have been shown to work because of poor oral absorption, rapid elimination *in vivo*, and unwanted activity at other GPCRs (pages 791-792).

Ness et al. (*Expert Opinion in Therapeutic Patents*, **2006**, *16(8)*, 1051-65) teach that *in vivo* binding of CCR5 receptors is unpredictable because many of the antagonists lack specificity, interaction with muscarinic receptors and/or other chemokine receptors. Redundancy that is apparent *in vitro* may not appear *in vivo* (evidence supports non-redundant roles for two CCR5 ligands, CCL3 and CCL5) (page 1060).

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position. The relative skill of those in

this art is MD's, PhD's, or those with advanced degrees and the requisite experience in binding studies of compounds with CCR1 and CCR5 receptors.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for *in vitro* binding of compounds of formula I to CCR1 and CCR5 receptors.

However, the specification does not provide guidance for treatment of disease related to binding of CCR1 or CCR5.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claim 15 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

9. Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for simple compositions comprising compounds of formula I, does not reasonably provide enablement for complex compositions of compounds of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether

undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to compounds composed of a piperidine ring connected to a phenyl ring, which is further modified with an alkylene-amide-phenyl group, and simple and complex compositions comprising the same. Thus, the claims taken together with the specification imply complex compositions comprising compounds of formula I can be formed.

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position. The relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in preparation of complex compositions.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for simple compositions comprising compounds of formula I.

However, the specification does not provide guidance for complex compositions comprising compounds of formula I. What is the ratio of active compounds in complex compositions in the instant case? Applicants provide no examples of

these compositions. Therefore, it is difficult to determine how the complex compositions can be formed.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 17 and 18 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, 3, 9-15, and 17-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In a compound of formula I, what substituent(s) is/are intended for rings B and D? What substituent(s) is/are intended for variable J? What cyclic group(s) is/are intended to act as substituent(s) for a C1-6 alkyl group, C2-6 alkenyl group, or a C2-6 alkynyl group? In claims 17 and 18, what additional specific agents are intended in combination with a compound of formula I? Each recited agonist or inhibitor represents a broad class of compounds. In the specification, the definitions for these agents are open-ended. Thus, it unclear what specific agents are intended in this claim. In claim 18, what specific disease is being treated by administration of the complex composition?

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 1, 3, and 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buhr et al. (WO2003093297, published November 13, 2003).

Determining the scope and contents of the prior art

Buhr et al. teach compound 200 (page 39). In this compound, variable A is piperidine, ring B is phenylene, G is CH_2-J is NHC(O), and ring D is phenyl substituted at its *meta* position with 2-C(O)NHMe)-3-amino-pyrazin-6-yl. Compositions comprising this compound are taught from paragraph 0149 through 0162 (pages 93-96).

Ascertaining the differences between the prior art and the claims at issue

In formula I of claim 1, variable R^1 can be a C1-6 alkyl group. In compound 200, variable R^1 is H.

Resolving the level of ordinary skill in the pertinent art

One of ordinary skill in the art recognizes that H is a homologue of methyl because these two groups only differ by a CH_2 linkage.

Considering objective evidence present in the application indicating obviousness or nonobviousness

Sterling Drug Inc. v. Watson, Comr. Pats. (108 USPQ 37) teaches: "Test in determining patentability of compound that is homologue of another is whether its beneficial characteristics are both unexpected and obvious."

In the instant case, because the compounds are structurally similar (except for variable R^1), it would be obvious to try compound 200 in Buhr et al. in the same intended use as the instant application.

15. Claims 1, 3, and 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Priepke et al. (WO200204403, published January 17, 2002).

Determining the scope and contents of the prior art

Priepke et al. teach beispiel 42 (pages 50-51). In beispiel 42, variable A is piperidine, ring B is phenylene, G is CH_2-J is NHC(O), and ring D is phenyl substituted at its *meta* position with NHC(O)phenylene-*o*-4-trifluoromethyl-benzene. Compositions comprising this compound are taught in the abstract.

Ascertaining the differences between the prior art and the claims at issue

In formula I of claim 1, variable R^1 can be a C1-6 alkyl group. In beispiel 42, variable R^1 is H.

Resolving the level of ordinary skill in the pertinent art

One of ordinary skill in the art recognizes that H is a homologue of methyl because these two groups only differ by a CH_2 linkage.

Considering objective evidence present in the application indicating obviousness or nonobviousness

Sterling Drug Inc. v. Watson, Comr. Pats. (108 USPQ 37) teaches: "Test in determining patentability of compound that is homologue of another is whether its beneficial characteristics are both unexpected and obvious."

In the instant case, because the compounds are structurally similar (except for variable R^1), it would be obvious to try the compound of beipsiel 42 in Priepke et al. in the same intended use as the instant application.

16. Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Effenberger et al. (*Chemische Berichte*, **1972**, *105(6)*, 1926-42).

Determining the scope and contents of the prior art

Effenberger et al. teach compounds 3t and 3w (page 1929). In each of these compounds, ring A is piperidine, ring B is a phenylene ring substituted with an OH group, variable G is C(O) (substituted alkylene), variable J is NHC(O), and ring D is phenyl.

Ascertaining the differences between the prior art and the claims at issue

In formula I of claim 1, variable R^1 can be a C1-6 alkyl group. In compounds 3t and 3w, variable R^1 is H.

Resolving the level of ordinary skill in the pertinent art

One of ordinary skill in the art recognizes that H is a homologue of methyl because these two groups only differ by a CH_2 linkage.

Considering objective evidence present in the application indicating obviousness or nonobviousness

Sterling Drug Inc. v. Watson, Comr. Pats. (108 USPQ 37) teaches: "Test in determining patentability of compound that is homologue of another is whether its beneficial characteristics are both unexpected and obvious."

In the instant case, because the compounds are structurally similar (except for variable R^1), it would be obvious to try compounds 3t and 3w of Effenberger et al. in the same intended use as the instant application.

Double Patenting

17. Claims 10-14 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 9. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 9-14 are each compound claims. Because the intended use does not carry any patentable weight, claims 10-14 are considered duplicates of claim 9.

Conclusion

18. No claims are allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624